Chemotherapy Protocol

LYMPHOMA

CHLORAMBUCIL-PREDNISOLONE-PROCARBAZINE-VINBLASTINE

(ChlVPP)

Regimen

- Lymphoma – ChlVPP-Chlorambucil-Prednisolone-Procarbazine-Vinblastine

Indication

- Hodgkin's Lymphoma

Toxicity

Drug	Adverse Effect
Chlorambucil	Gastro-intestinal disturbance
Prednisolone	Weight gain, gastro-intestinal disturbances, hyperglycaemia, CNS disturbances, cushingoid changes, glucose intolerance
Procarbazine	Insomnia, ataxia, hallucinations, headache
Vinblastine	Peripheral neuropathy, constipation, jaw pain, ileus

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Patients diagnosed with Hodgkin's Lymphoma carry a lifelong risk of transfusion associated graft versus host disease (TA-GVHD). Where blood products are required these patients must receive only irradiated blood products for life. Local blood transfusion departments must be notified as soon as a diagnosis is made and the patient must be issued with an alert card to carry with them at all times.

Monitoring

Drugs

- FBC prior to day one and eight of treatment
- LFTs and U&Es prior to day one of treatment

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and limited drug specific toxicities. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

Haematological

Dose modifications for haematological toxicity in the table below are for general guidance only. Always refer to the responsible consultant as any dose reductions or delays will be dependent on clinical circumstances and treatment intent. Low counts can be a consequence of bone marrow infiltration as well as drug toxicity.

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL. **Irradiated blood products must be used in Hodgkin's Lymphoma patients.**

Day One

Neutrophils ($x10^9$/L)	**Dose Modifications**
1.5 or greater	100%
less than 1.5	Delay until recovery
Platelets ($x10^9$/L)	**Dose Modifications**
100 or greater	100%
less than 100	Delay until recovery

Day Eight

Neutrophils ($x10^9$/L)	**Dose Modifications**
0.5 - 1	Reduce the chlorambucil and vinblastine dose to 50%. Stop the procarbazine.
less than 0.5	Omit the vinblastine. Stop the chlorambucil and procarbazine.
Platelets ($x10^9$/L)	**Dose Modifications**
50 - 80	Reduce the chlorambucil and vinblastine dose to 50%. Stop the procarbazine.
less than 50	Omit the vinblastine. Stop the chlorambucil and procarbazine

Hepatic Impairment

Please note that the approach may be different where abnormal liver function tests are due to disease involvement.

Drug	Bilirubin (µmol/L)		AST/ALT (units/L)	Dose (% of original dose)
Chlorambucil				Dose reduce in severe hepatic impairment
Procarbazine	more than 50			Consider dose reduction
	more than 85	or	more than 180	Omit
Vinblastine	*30-51	or	60-180	50%
	more than 51	and	normal	50%
	more than 51	and	more than180	Omit

* Limits reflect local practice and may vary from published sources

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Chlorambucil		No dose adjustment needed
Procarbazine	more than 177 µmol/L	50%
	less than 10	Not recommended
Vinblastine	N/A	No dose adjustment needed

Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

Vinblastine

Reduce the vinblastine dose to 3mg/m^2 if a NCI-CTC grade 2 motor or a NCI-CTC grade 3 sensory neurological toxicity occurs. For higher toxicity grades or if toxicity increases despite dose reduction stop the vinblastine.

Regimen

28 day cycle for 6 cycles

Drug	Dose	Days	Administration
Chlorambucil	6mg/m^2 (max 10mg)	1-14	Oral
Prednisolone	40mg	1-14	Oral
Procarbazine	100mg/m^2 (max 200mg)	1-14	Oral
Vinblastine	6mg/m^2 (max 10mg)	1 and 8	Intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

Dose Information

- Chlorambucil is available as 2mg tablets and will be rounded to the nearest 2mg (up if halfway)
- Chlorambucil tablets should be stored in a refrigerator
- Vinblastine dose will be rounded to the nearest 1mg (up if halfway)
- The maximum dose of vinblastine is 10mg.
- Prednisolone is available as 5mg and 25mg tablets
- Procarbazine is available as 50mg capsules. The daily dose will be capped at 200mg. To facilitate alternate day dosing in ARIA the dose will be rounded to the nearest 25mg (up if halfway).
    - If the calculated daily dose is 125mg please dispense 150mg alternating with 100mg daily
    - If the calculated daily dose is 175mg please dispense 200mg alternating with 150mg daily

Administration Information

Extravasation

- Vinblastine - vesicant

Other

- Chlorambucil may be taken at night to avoid daytime nausea
- Prednisolone should be taken in the mornings with or after food
- Procarbazine has weak MAOI activity. Alcohol and foods rich in tyramine (including some wines and cheeses) should be avoided. Do not use with other MAOIs.

Additional Therapy

- Antiemetics

15-30 minutes prior to chemotherapy

  - metoclopramide 10mg oral or intravenous

As take home medication day 1 only

  - metoclopramide 10mg oral three times a day when required

- Allopurinol 300mg once a day oral for the first cycle only
- Consider anti-infective prophylaxis in high risk patients including:

  - aciclovir 400mg twice a day oral
  - co-trimoxazole 960mg once a day on Monday, Wednesday and Friday only oral

- Mouthwashes according to local or national policy on the treatment of mucositis
- Gastric protection with a proton pump inhibitor or a H_2 antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

Additional Information

- The National Patient Safety Agency report NPSA/2008/RRR04 must be followed in relation to intravenous administration of vinca alkaloids.
- The National Patient Safety Agency alert NPSA/2008/RRR001 must be followed when prescribing, dispensing or administering oral chemotherapy.
- It must be made clear to all staff, including those in the community, that this is a short course of oral chemotherapy that must not be continued.
- Patients should be assessed for suitability for oral chemotherapy prior to starting treatment.

Coding (OPCS 4.6)

- Procurement – X70.3
- Delivery – X72.3 Day 1 + X72.4 Day 8

References
1.ChlVPP therapy for Hodgkin's Disease: experience of 960 patients. The International ChlVPP Treatment Group. Ann. Oncol. 1995;6(2):167-172
2.McBwain TJ, Toy J, Smith E et al. A combination of chlorambucil, vinblastine, procarbazine and prednisolone for treatment of Hodgkin's disease. Br J Cancer 1977;36(2):276-285
3.Selby P, Patel P, Milan S et al. ChlVPP combination chemotherapy for Hodgkin's disease: long-term results. Br J Cancer 1990; 62 (2); 279-285

REGIMEN SUMMARY

ChlVPP-Chlorambucil-Prednisolone-Procarbazine-Vinblastine

Cycle 1 Day One

1. Warning –Check blood transfusion status
   Administration Instructions
   Patients with HODGKIN'S lymphoma carry a lifelong risk of transfusion associated graft versus host disease.
   Where blood products are required these patients must receive ONLY IRRADIATED BLOOD PRODUCTS for life.
   Ensure transfusion departments are notified and the patient has been issued with an alert card to carry with them at all times.

2. Metoclopramide 10mg oral or intravenous

3. Vinblastine 6mg/m^2 (max 10mg) intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

Take Home Medicines

4. Chlorambucil 6mg/m^2 (max 10mg) once a day oral for 14 days

5. Prednisolone 40mg once a day oral for 14 days

6. Procarbazine 100mg/m^2 (max 200mg) once a day oral for 14 days

7. Allopurinol 300mg once a day oral for 28 days

8. Metoclopramide 10mg three times a day oral when required

Cycle 1 Day Eight

1. Metoclopramide 10mg oral or intravenous

2. Vinblastine 6mg/m^2 (max 10mg) intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

Cycles 2, 3, 4, 5 & 6 Day One

1. Metoclopramide 10mg oral or intravenous

2. Vinblastine 6mg/m^2 (max 10mg) intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

Take Home Medicines

1. Chlorambucil 6mg/m^2 (max 10mg) once a day oral for 14 days

2. Prednisolone 40mg once a day oral for 14 days

3. Procarbazine 100mg/m^2 (max 200mg) once a day oral for 14 days

4. Metoclopramide 10mg three times a day oral when required

Cycles 2, 3, 4, 5 & 6 Day Eight

1. Metoclopramide 10mg oral or intravenous

2. Vinblastine 6mg/m^2 (max 10mg) intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.1	Jan 2015	Header changed Toxicities removed Hepatic impairment table updated Metoclopramide dose changed to 10mg Bolus removed from intravenous bolus throughout text cIrradiated blood product statement updated in dose modification section. Mucositis recommendation changed OPCS code updated "Warning-Check blood transfusion status" added to cycle 1 Disclaimer added	Donna Kimber Pharmacy Technician	Rebecca Wills Pharmacist
1	May 2012	None	Rebecca Wills Pharmacist Dr Debbie Wright Pharmacist	Dr Andrew Davies Consultant Medical Oncologist Dr Alison Milne Consultant Haematologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury Hospitals NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.